Complete Summary

GUIDELINE TITLE

Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 23 p. (Technology appraisal guidance; no. 107).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2005, Herceptin (trastuzumab): Healthcare professionals were notified of updated cardiotoxicity information related to use.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Early-stage human epidermal growth factor-like receptor No. 2 (HER2)-positive breast cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Internal Medicine
Obstetrics and Gynecology
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of trastuzumab for the treatment of early-stage human epidermal growth factor-like receptor No. 2 (HER2)-positive breast cancer

TARGET POPULATION

Patients with early-stage human epidermal growth factor-like receptor No. 2 (HER2)-positive breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Trastuzumab (Herceptin) following surgery, chemotherapy, and radiotherapy
2. Assessment of cardiac function prior to treatment and every 3 months

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Overall and disease-free survival
    - Cancer recurrence
    - Adverse events
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The report for this technology appraisal was prepared by the School of Health and Related Research (ScHARR), University of Sheffield (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of Manufacturer's Approach

Description of Manufacturer's Search Strategy

The manufacturer's searches, conducted in December 2005, were restricted to publications from 1993 onwards. Whether and how restrictions were placed on the searches is not clear. The searches were simple and relied heavily on Medical Subject Headings (MeSH) without support from free-text terms. There was also inconsistency between searches of different databases. For instance, some used 'trastuzumab' and 'herceptin' as search term, whilst others just used 'trastuzumab'. Nevertheless, the search strategies were adequate to retrieve important citations relating to all eligible studies of which the ERG and its clinical advisors are aware.

Statement of the Inclusion/Exclusion Criteria Used

Restrictions to studies on the adjuvant use of trastuzumab (and synonyms) in humans with early breast cancer and (given the timescale) English language publications were appropriate.

Restriction to 'clinical trial data publications' (presumably meaning '*controlled* clinical trials' – those with comparator arms) is appropriate for the assessment of clinical benefit. However, the reporting of clinical harms is often inadequate in controlled clinical trial publications because they exclude patients at high risk from harms, may be too short to identify long-term or delayed harms, or may have sample sizes too small to detect uncommon events.

Identified Studies

The manufacturer's submission identified five relevant phase III clinical trials of which the ERG are aware.

Refer to the ERG Report (see the "Availability of Companion Documents" field) for the critique of the manufacturer's approach to study exclusions.

Details of Any Relevant Studies That Were Not Included in the Submission

Between the 9th and 28th March, 2006, the ERG re-ran the manufacturer's searches. No further Phase III controlled trials were found when the search results were screened.

NUMBER OF SOURCE DOCUMENTS

The manufacturer's submission identified the five relevant phase III clinical trials of which the Evidence Review Group (ERG) are aware:

The manufacturer's submission excluded FinHER study from the review.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The report for this technology appraisal was prepared by the School of Health and Related Research (ScHARR), University of Sheffield (see the "Availability of Companion Documents" field).

Critique of Manufacturer's Approach

Clinical Effectiveness

Critique of Submitted Evidence Syntheses

The Strength of the Evidence (Internal Validity)

The search strategy was poorly designed (see the "Description of Methods Used to Collect/Select the Evidence" field) but the ERG have not determined that any relevant primary studies were missed as a result. The inclusion criteria were adequately defined, but the manufacturer's study selection and use of the published evidence seemed to work on a highly selective and arbitrary basis, in the reporting of outcome data (Sections 4.1.3, 4.1.6 and 4.1.7 of the ERG Report [see the "Availability of Companion Documents" field]). The manufacturer's approach to validity assessment appears to have been adequate, but the template they were asked to use by NICE has problems (Section 4.1.5 of the Assessment Report). The manufacturer's reporting of secondary outcomes, particularly adverse events was somewhat haphazard (Section 4.2.4.1 of the ERG Report).

Critical outcomes used in the model were poorly defined in the manufacturer's submission and not reported in the public domain. As the review team could not access the individual patient data from the pivotal trial, they are unable to validate the manufacturer's analysis of this data. Where comparisons with similar published outcomes are possible there is no evidence of any inexplicable discrepancies (Section 3.4.1 of the Assessment Report [see the "Availability of Companion Documents" field]).

Time is an important factor in breast cancer, which has a long natural history, with recurrences occurring out beyond 20 years. The median follow-up in the pivotal trial is only one year. Many consider disease-free survival a surrogate for long-term, all-cause mortality in breast cancer. This has only been empirically demonstrated in other classes of treatment (standard cytotoxics and tamoxifen). The manufacturer reasons, by analogy alone, that the empirically known, short-term harm-benefit profile of trastuzumab will result in a long-term harm-benefit profile similar to that empirically known for other classes of drug (Sections 3.5, 4.1.7 and 4.1.8.2 of the ERG Report).

The Applicability of the Results (External Validity)

Women at elevated risk of a cardiac event were not recruited to the clinical trials which evaluated trastuzumab (Sections 3.1.2 and 4.3.2 of the ERG Report [see the "Availability of Companion Documents" field]) .Those women who were recruited were intensively monitored. This puts the onus (and the additional cost of screening) on the National Health Service (NHS) to replicate an eligible population for whom the treatment will be as safe as in the clinical trials. If the current shortfall in cardiac monitoring capacity is not adequately addressed, women treated with trastuzumab will be at elevated risk of heart failure compared with those in the clinical trials.

A restrictive scope allowed the manufacturer to exclude from any serious discussion the FinHer study (Section 4.1.3.2 of the ERG Report [see the "Availability of Companion Documents" field]). The manufacturer rightly pointed out that the underlying anthracycline-containing regimen was different to any used in the NHS. However, cancer clinicians have noted that the nine week regimen examined in this study may facilitate lower cost, greater patient convenience, and reduced risk of cardiotoxicity, although the evidence is not as strong as that for 52 weeks.

Considerable heterogeneity of study populations in terms of the concomitant chemotherapies received and lack of knowledge about what regimens are in use in the NHS make generalisation from the published evidence problematic (Section 3.3.1, 3.3.2 of the ERG Report [see the "Availability of Companion Documents" field]), although the direction and extent of clinical effect seems relatively consistent across different baseline treatment programmes.

Cost-Effectiveness

Overview of Manufacturer's Economic Evaluation

A state transition cohort model was used to compare the lifetime impact of one year of adjuvant trastuzumab therapy to no trastuzumab following standard chemotherapy regimens based on the Herceptin Adjuvant (HERA) trial. The clinical effectiveness aspect of the model is based upon the HERA trial1 which was an international, multi-centre, randomised trial on women with HER2 positive primary breast cancer.

Additional Work Undertaken by the ERG

Clinical Effectiveness

The ERG carried out the following analyses which the manufacturer declined to undertake: (1) a meta-analysis of trials to derive a more precise estimate of treatment effect in terms of overall survival (Section 7.1.1 of the ERG report [see the "Availability of Companion Documents" field]), disease-free survival (Section 7.1.2 of the ERG Report), distant recurrence (Section 7.1.3 of the ERG Report) and cardiac toxicity (Section 7.1.4) of the ERG Report; and, (2) a critical evaluation of the role of the FinHer study in decision-making (Section 7.1.5 of the ERG Report).

For time-to-event outcomes, summary statistics from the published literature were meta-analysed using the method described by Parmar, Torri, & Stewart, (1998) with a fixed effects model. Heterogeneity between trial results was tested using the chi^2 test and the I^2 measurement. The chi^2 test measures the amount of variation in a set of trials. Small p values ($p<0.10$) suggest that there is more heterogeneity present than would be expected by chance. I^2 is the proportion of variation that is due to heterogeneity, rather than chance. Large values of I^2 suggest heterogeneity. I^2 values of 25%, 50%, and 75% could be interpreted as representing low, moderate, and high heterogeneity.

The Absolute Risk Reduction (ARR) and Numbers Needed to Treat for time-to-event outcomes were calculated using methods described by Altman and Andersen (1999). This method uses the numbers of patients still at risk (alive) at the time corresponding to the estimated probabilities (reported or imputed), or hazard ratios and 95% confidence intervals, to calculate confidence intervals for each statistic.

Cost-Effectiveness

As a result of the communication with Roche, the ERG has developed what they believe to be a reasonable revised base-case. Sensitivity analysis has also been carried out to ensure that the model results are robust. The analysis is described in Section 7.2 of the ERG Report (see the "Availability of Companion Documents" field).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Committee reviewed the evidence on the cost effectiveness of trastuzumab. It was aware that limitations in the evidence base meant that a number of assumptions were made in the manufacturer's economic model. The Committee heard that as yet there is no evidence from trastuzumab trials of the duration of benefit following 1 year of trastuzumab treatment. It reflected that, on the basis of evidence from trials of other chemotherapy agents for high-risk early-stage breast cancers, the assumption of a lifetime benefit made in the manufacturer's model was likely to be optimistic and that a more conservative assumption would be 5 years of clinical benefit. In addition the Committee heard from the clinical specialists that the assumption by the manufacturer that women who had received trastuzumab in the adjuvant setting would not then receive trastuzumab in the metastatic setting was unlikely to reflect clinical practice. The Committee concluded that, based on these assumptions, the incremental cost per quality adjusted life year (QALY) estimate of 2,387 pounds sterling in the manufacturer's submission was likely to be underestimated and that the evidence review group's estimate of 18,000 pounds sterling was more likely to reflect the cost effectiveness of trastuzumab. However, it was mindful that the latter was also associated with uncertainty and that the alternative assumption that 100% of patients would be re-treated with trastuzumab for metastatic breast cancer, as proposed by the evidence review group, was also unlikely to fully reflect clinical practice.

The Committee considered how cardiac adverse events had been included in the cost-effectiveness estimates from the manufacturer. In the manufacturer's model it was assumed that severe (grade 3 and 4) and less severe (grade 1 and 2) cardiac adverse effects occurred at the same rate as in the Herceptin Adjuvant (HERA) trial and only occurred during treatment with trastuzumab. In addition, the model assumed there was no mortality associated with any cardiac event in either the short or long term. Therefore the Committee considered that the manufacturer's model underestimated both the costs and the reduction in quality of life associated with the treatment of possible long-term effects of cardiotoxicity. The Committee considered the sensitivity analysis carried out by the evidence review group that assumed that 23% of women would experience a cardiac event

following treatment with trastuzumab, as is known to occur with anthracycline-including chemotherapy regimens. All other assumptions were maintained in the analysis. The Committee noted that the resulting estimate of cost per QALY gained would be approximately 33,000 pounds sterling and that this also assumed no excess mortality.

The Committee was mindful that the favorable cost per QALY estimates could have been a function of the extensive cardiac screening, monitoring and treatment discontinuation rules used in the Herceptin Adjuvant (HERA) study before and during trastuzumab treatment which would therefore need to be replicated in clinical practice. The Committee was also aware of the possibility that, although no direct evidence was presented, estimates of cost per QALY gained for those patients with significant cardiac risk factors who were excluded from the registration trial, in particular women with a left ventricular ejection fraction (LVEF) of 55% or less, could reasonably be assumed to be higher than both the manufacturer's estimates and the base–case suggested by the evidence review group. The Committee concluded that on this basis it would not be able to recommend trastuzumab for patients who have an LVEF of 55% or less or one of a documented range of cardiac conditions as specified in the exclusion criteria of the registration trial and identified in the summary of product characteristics (SPC).

Refer to Section 4 of the original guideline document for more information on cost effectiveness.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), is recommended as a treatment option for women with early-stage human epidermal growth factor-like receptor No 2

(HER2)-positive breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant), and radiotherapy (if applicable).

- Cardiac function should be assessed prior to the commencement of therapy and trastuzumab treatment should not be offered to women who have a left ventricular ejection fraction (LVEF) of 55% or less, or who have any of the following:
    - A history of documented congestive heart failure
    - High-risk uncontrolled arrhythmias
    - Angina pectoris requiring medication
    - Clinically significant valvular disease
    - Evidence of transmural infarction on electrocardiograph (ECG)
    - Poorly controlled hypertension
- Cardiac functional assessments should be repeated every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50% then trastuzumab treatment should be suspended. A decision to resume trastuzumab therapy should be based on a further cardiac assessment and a fully informed discussion of the risks and benefits between the individual patient and their clinician.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of trastuzumab for the treatment of early-stage breast cancer in human epidermal growth factor-like receptor No.2 (HER2) positive women

POTENTIAL HARMS

Trastuzumab is associated with cardiotoxicity.

For full details of the side effects and contraindications see the summary of product characteristics (SPC) available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

The "Summary of Produce Characteristics" (SPC) states that treatment cannot be recommended for patients with a history of documented congestive heart failure,

high-risk uncontrolled arrhythmias, angina pectoris requiring medication, clinically significant valvular disease, evidence of transmural infarction on electrocardiograph (ECG), or poorly controlled hypertension, because these patient groups were excluded from the registration study. The SPC also states that caution should be taken in treating patients with symptomatic heart failure, a history of hypertension, documented coronary artery disease, or a left ventricular ejection fraction (LVEF) of 55% or less.

For full details of the side effects and contraindications see the summary of product characteristics (SPC) available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Weaknesses of cost effectiveness evidence submitted by the manufacturer:
    - No sensitivity analysis has been undertaken to explore the impact of uncertainty surrounding the comparator arm on the incremental cost-effectiveness ratio (ICER).
    - Little sensitivity analysis has been carried out around the long-term benefits of trastuzumab.
    - Confidence intervals of some of the parameters do not adequately describe the uncertainty. For instance, the upper values of the cost of trastuzumab and cardiac monitoring were considered to be unrealistic.
- Areas of uncertainty:
    - Disease-free and overall survival may differ from the comparator arm in the model, depending on the chemotherapy regimens being used in the United Kingdom (UK).
    - The benefits of trastuzumab on rates of recurrence are unknown beyond three to four years.
    - There is little evidence to date of the effects of trastuzumab upon overall survival.
    - There is no evidence of the effects of trastuzumab upon long term cardiac dysfunction.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by

National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.

- "Healthcare standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (www.nice.org.uk).
    - Costing report and costing template to estimate the savings and costs associated with implementation
    - Audit criteria to monitor local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. London (UK):

National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 23 p. (Technology appraisal guidance; no. 107).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Aug

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 2 p. (Technology appraisal 107). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Costing template and report: trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. Various p. (Technology appraisal 107). Available in Portable Document Format (PDF) from the NICE Web site.
- Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 14 p. (Technology appraisal 107). Available in Portable Document Format (PDF) from the NICE Web site.
- Trastuzumab for the treatment of primary breast cancer in HER2 positive women: a single technology appraisal. Evidence Review Group Report. School of Health and Related Research (ScHARR), University of Sheffield, UK. 2006 May. 123 p. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1111. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 4 p. (Technology appraisal 107).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site. Also available in Welsh from the NICE Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1112. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on August 1, 2007.

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